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SERIAL NUMBER	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
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18N1/1101

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EXAMINER	
ART UNIT	PAPER NUMBER
1818	4

DATE MAILED: 11/01/95

This is a communication from the examiner in charge of your application.
COMMISSIONER OF PATENTS AND TRADEMARKS

☒ This application has been examined ☐ Responsive to communication filed on _____ ☐ This action is made final.

A shortened statutory period for response to this action is set to expire 3 month(s), 0 days from the date of this letter.
Failure to respond within the period for response will cause the application to become abandoned. 35 U.S.C. 133

Part I THE FOLLOWING ATTACHMENT(S) ARE PART OF THIS ACTION:

1. ☒ Notice of References Cited by Examiner, PTO-892.
2. ☒ Notice of Draftsman's Patent Drawing Review, PTO-948.
3. ☐ Notice of Art Cited by Applicant, PTO-1449.
4. ☐ Notice of Informal Patent Application, PTO-152.
5. ☐ Information on How to Effect Drawing Changes, PTO-1474.
6. ☐ _____

Part II SUMMARY OF ACTION

1. ☒ Claims 1-19 are pending in the application.
   Of the above, claims _____ are withdrawn from consideration.
2. ☐ Claims _____ have been cancelled.
3. ☐ Claims _____ are allowed.
4. ☒ Claims 1-19 are rejected.
5. ☐ Claims _____ are objected to.
6. ☐ Claims _____ are subject to restriction or election requirement.
7. ☐ This application has been filed with informal drawings under 37 C.F.R. 1.85 which are acceptable for examination purposes.
8. ☐ Formal drawings are required in response to this Office action.
9. ☐ The corrected or substitute drawings have been received on _____. Under 37 C.F.R. 1.84 these drawings are ☐ acceptable; ☐ not acceptable (see explanation or Notice of Draftsman's Patent Drawing Review, PTO-948).
10. ☐ The proposed additional or substitute sheet(s) of drawings, filed on _____. has (have) been ☐ approved by the examiner; ☐ disapproved by the examiner (see explanation).
11. ☐ The proposed drawing correction, filed _____, has been ☐ approved; ☐ disapproved (see explanation).
12. ☐ Acknowledgement is made of the claim for priority under 35 U.S.C. 119. The certified copy has ☐ been received ☐ not been received ☐ been filed in parent application, serial no. _____ ; filed on _____.
13. ☐ Since this application apppears to be in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under Ex parte Quayle, 1935 C.D. 11; 453 O.G. 213.
14. ☐ Other

EXAMINER'S ACTION

15. The disclosure is objected to because of the following informalities: the claims should begin with "I claim", "We claim" or "What is claimed is", page 19, line 15, "titiers", should be "titers", page 15, line 19, "difference " should be plural, page 17, line 19, "permiabilize", should be "permeabilize. Appropriate review and correction of the entire specification are required.

16. The figures are objected to under 37 CFR 1.84 for reasons specifically outlined in the accompanying PTO Form 948.

17. Claims 5, 6, 18 are objected to under 37 C.F.R. § 1.75(c) as being in improper form because a multiple dependent claim shall not serve as a basis for any other multiple dependent claim.. See M.P.E.P. § 608.01(n). Accordingly, claims 5 and 6 are being viewed as if they depended from claim 1 and claim 18 is being viewed as if it depended from claim 10.

18. Claims 1-19 are provisionally rejected under 35 U.S.C. 101 as claiming the same invention as that of claims 1-19 of copending application Serial No. 08/470, 107 and claims 1-19 of copending application serial number 08/459,147. This is a *provisional* double patenting rejection since the conflicting claims have not in fact been patented.

19. Claims 7, 11, 13, 18, and 19 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1, 2, 10, 13, 14,

17, 20-23 of copending application Serial No. 08/357,084. Although the conflicting claims are not identical, they are not patentably distinct from each other because the claims are drawn to the glycoprotein D of herpes simplex virus and methods of producing the glycoprotein in continuous cell culture.

This is a *provisional* obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

The non-statutory double patenting rejection, whether of the obvious-type or non-obvious-type, is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent. *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); *In re Van Ornam*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); and *In re Goodman*, 29 USPQ2d 2010 (Fed. Cir. 1993).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321 (b) and (c) may be used to overcome an actual or provisional rejection based on a non-statutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.78 (d).

Effective January 1, 1994, a registered attorney or agent of record may sign a Terminal Disclaimer. A Terminal Disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

20. Claims 1-19 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The language of the claim is not as precise as the subject matter permits such that one may reasonably know what will infringe and what will not infringe the

claims. The claims are indefinite in the recitation of "antigenic determinant" because it is unclear what applicant intends. Claim 6 is indefinite because it is not clear whether or not applicant intended the word "at" to be deleted or the terminology "at least one" from the claim. Claim 13 is indefinite because it is unclear whether or not applicant intends the truncated polypeptide to contain amino acids 1-300. Clarification is required in order to overcome this rejection.

21. Claims 1-6, 8, 9, 10, 12, 13, 14-17 are rejected under 35 U.S.C. § 112, first paragraph, as the disclosure is enabling only for claims limited a vaccine comprising a membrane associated and truncated form of the herpes simplex glycoprotein D and a method of producing the herpes simplex glycoprotein D vaccine. See M.P.E.P. §§ 706.03(n) and 706.03(z).

The claims are very broadly drawn to a vaccine comprising membrane-bound and membrane-free polypeptides from a pathogen capable of raising neutralizing antibodies to any pathogen. The examiner views the broad claims as encompassing all bacterial, viral, fungal and protozoan species. The specification lacks sufficient guidance and teaching to enable the entire scope of the claims. Moreover, the specification lacks sufficient guidance and teaching to enable the use of the glycoprotein C from herpes simplex virus. Indeed the specification states on page 46 that the function of the glycoprotein C is unknown and

that it is not clear that gC is indispensable to the viruses during in vivo infection of the human and the establishment of latency. While the specification describes sequence homologies between gC and gF, the specification lacks enablement to show a correlation between gC and gD, such that one might reasonably expect similarity in structure and function. Thus it would appear that the role of the gC glycoprotein in generating protective immune responses has also not been clearly defined and one would not be able to reasonably predict success with a vaccine against herpes simplex virus comprising the glycoprotein C absence evidence of its function. In view of all of the above, it is determined that the specification is not commensurate in scope with the claimed subject matter.

22. Upon review of all of the parent applications there appears to be no support for the scope of the invention as is now claimed. Therefore the following will apply to the specified claims:

a) claims 7, 11, 13, 18 and 19 are entitled to a filing date of 8/30/83 and

b) claims 1-6, 8-10, 12, 14-17 are entitled to a filing date of 6/2/95 (the filing date of the instant application). references published prior to 8/30/83 will be considered as valid prior art for claims 7, 11, 13, 18 and 19 and references

published prior to 6/2/95 will be considered as valid prior art for claims 1-6, 8-10, 12 and 14-17.

The following is a quotation of the appropriate paragraphs of 35 U.S.C. § 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

23. Claims 1-6, 10, 14-17 are rejected under 35 U.S.C. § 102(b) as being anticipated by Berman, 1988. The claims are very broadly drawn to a vaccine comprising membrane-associated and truncated forms of a polypeptide capable of raising neutralizing antibodies to a pathogen. The claims are not limited to a particular pathogen and do not exclude the present of other ingredients in the vaccine. The examiner is interpreting the claims to read on any polypeptide from any pathogen.

Berman et al describe the expression of membrane-associated and secreted variants of gp160 of the human immunodeficiency virus type 1 in continuous eucaryotic cell lines (abstract and page 3137). The membrane-associated and secreted forms of the glycoprotein were expressed in the mammalian CHO cell line which was deficient in dhfr (page 3136, second column). The signal sequence of the HIV-1 envelope glycoprotein was deleted (page 3137-3138, figures 1 and 2) thus appearing to truncate the

HIV-1 polypeptide. Antibodies from infected patients reacted with the truncated protein D516 (page 3138, first column). The membrane-associated and truncated forms of the claimed polypeptide appear to be the same as the claimed membrane associated and truncated forms of the prior art polypeptide in that there appears to be exposed antigenic determinants present. The recitation of vaccine is being viewed by the examiner as an intended use and appears to impart no other distinguishing characteristics to the claimed polypeptide. This essentially describes the invention as claimed. Characteristics such as capabilities of raising neutralizing antibodies are being viewed by the examiner as "potential" which would be inherent in the polypeptides of the prior art reference.

The following is a quotation of 35 U.S.C. § 103 which forms the basis for all obviousness rejections set forth in this Office action:

> A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.
>
> Subject matter developed by another person, which qualifies as prior art only under subsection (f) or (g) of section 102 of this title, shall not preclude patentability under this section where the subject matter and the claimed invention were, at the time the invention was made, owned by the same person or subject to an obligation of assignment to the same person.

24. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. § 103, the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 C.F.R. § 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of potential 35 U.S.C. § 102(f) or (g) prior art under 35 U.S.C. § 103.

25. Claims ~~1-4, 6, 7,~~ 10, 11, 13-15, 18 and 19 are rejected under 35 U.S.C. § 103 as being unpatentable over Watson et al, 1982 in view of Rose et al, 1982. The claims are drawn to a vaccine comprising a herpes simplex membrane-bound and truncated glycoprotein D expressed in a continuous mammalian cell culture, which vaccine is capable of raising neutralizing antibodies and methods of producing the vaccine. The examiner is viewing the term vaccine as an intended use since it appears to impart no other distinguishing characteristics to the gD glycoprotein of herpes simplex virus.

Watson et al teach the cloning and expression of the gene coding for herpes simplex virus type 1 glycoprotein D. The glycoprotein D is capable of generating antiserum which can neutralize infectivity of herpes simplex virus (HSV) type 1 and

type 2. In vivo antiserum generated to the glycoprotein D protected mice from neurological disease induced by either HSV type 1 or type 2 (page 381). This was suggested to show "the potential for inducing immunity to infections of both HSV types with the use of a subunit vaccine consisting of a purified HSV-1 gD glycoprotein". The gD glycoprotein appears to be similar to the claimed membrane bound polypeptide. Also taught is the amino acid sequence of the gD glycoprotein (figure 2) including the signal sequence of the gD glycoprotein and the putative transmembrane region which appears around amino acid position 340 (page 382). It is stated that the signal sequence may be removed during translation (page 382). Watson et al also teach the construction of a glycoprotein D expression plasmid which appeared to have deleted 52 NH2-terminal amino acids from the gD glycoprotein (page 383, first column). Thus while Watson et al appear to describe a truncated gD glycoprotein, they differ from the claimed invention in not specifically describing a truncated secreted protein. However, Rose et al teach the expression of cell-surface secreted form of the vesicular stomatitis virus G protein which appears to be the model for integral plasma-membrane proteins (page 753). The G protein has the characteristic transmembrane domain and cytoplasmic domain and the truncated form of the G protein lacked these domains (page 754, second column). Expression of the truncated

polypeptide did result in secretion of the polypeptide into the medium, although the rate was somewhat slow (page 758). However, the claims are not drawn to the rate of transport of the polypeptide. Thus it would have been obvious to one of ordinary skill in the art at the time the invention was made to express the glycoprotein D molecule either as a membrane glycoprotein or as a secreted glycoprotein (for ease in recovery from the cell culture medium) in a vaccine composition. It would have been expected, barring evidence to the contrary, that the glycoprotein D, either membrane bound or secreted, would be effective in a vaccine composition in generating neutralizing antibody responses, when administered. Additionally, given the sequence of the HSV glycoprotein D as depicted by Watson showing the transmembrane sequence and the suggestion by Rose of deleting the signal sequence as well as the transmembrane domain, one would have a reasonable expectation of success in generating a truncated glycoprotein wherein the first NH2-terminal 300 amino acids are present.

26. Papers related to this application may be submitted to Group 180 by facsimile transmission. Papers should be faxed to Lynette F. Smith, Art Unit 1813 and should be marked "OFFICIAL" for entry into prosecution history or "DRAFT" for consideration by the examiner without entry. The Art Unit 1813 FAX telephone number is (703)-305-7939. FAX machines will be available to

receive transmissions 24 hours a day. In compliance with 1096 OG 30, the filing date accorded to each OFFICIAL fax transmission will be determined by the FAX machine's stamped date found on the last page of the transmission, unless that date is a Saturday, Sunday or Federal Holiday with the District of Columbia, in which case the OFFICIAL date of receipt will be the next business day.

27. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Lynette F. Smith whose telephone number is (703) 308-3909.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Smith/lfs
October 27, 1995

L. F. Smith
LYNETTE F. SMITH
PATENT EXAMINER
GROUP 1800